

Patent  
Attorney Docket No. 65731-76121

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

Claims 1 - 32 (Withdrawn).

33 (Currently amended): A method of screening for an agent which modulates ~~N-TAD~~ function of a protein comprising an amino acid of SEQ ID NO:5, comprising: incubating a mixture comprising:

an isolated protein ~~according to claim 29~~ comprising an amino acid of SEQ ID NO:4 with an altered PYI motif at residues 564-566;

a target protein; and

a candidate agent

under conditions whereby, but for the presence of said agent, said isolated protein specifically transactivates reporter genes, or mediates VHL-dependent degradation, or physically interacts with VHL at a reference affinity;

detecting the binding affinity of said isolated protein to said target protein to determine an agent-biased affinity;

wherein a difference between said reference affinity and said agent-biased affinity indicates that said agent modulates the functional activity of said isolated protein to said target protein.

34 (Original): The method of claim 33 wherein the target protein is VHL or a fragment thereof.

35 (Original): The method of claim 33 wherein the incubation is at normoxia.

36 (Original): The method of claim 33 wherein the incubation is at hypoxia.

Claims 37 - 39 (Withdrawn).

40 (Currently amended): A method of evaluating an antagonist of the PYI motif or ~~P564-spanning protein or a functional fragment thereof~~ a protein encoded by at least a fragment of SEQ ID NO:5 and comprising at least residue 33 of SEQ ID NO:5 for VHL-HIF-1 alpha interaction inhibiting efficacy, comprising: determining a reference ~~normal~~ level of VHL-HIF-1 alpha interaction in a cell, or a group of cells, ~~or an organism;~~

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administering said antagonist to an equivalent test cell, or a group of cells, ~~or an organism~~;  
measuring the level of VHL-HIF-1 alpha interaction in said test cell, or group of cells, ~~or organism~~; and  
determining said antagonist is efficacious when the measured test level of VHL-HIF-1 alpha interaction is less than the reference ~~normal~~ level of VHL-HIF-1 alpha interaction.

41 (Currently amended): The method of claim 40, wherein said test cell, or group of cells, ~~or organism~~ are at normoxia.

42 (Currently amended): The method of claim 40, wherein said test cell, or group of cells, ~~or organism~~ are at hypoxia.

Claims 43 - 66 (Withdrawn).